hereditary myopathy with early respiratory failure

Hereditary myopathy with early respiratory failure (HMERF) is an inherited muscle disease that predominantly affects muscles close to the center of the body (proximal muscles) and muscles that are needed for breathing.

The major signs and symptoms of HMERF usually appear in adulthood, on average around age 35. Among the earliest muscles affected in HMERF are the neck flexors, which are muscles at the front of the neck that help hold the head up. Other proximal muscles that become weak in people with HMERF include those of the hips, thighs, and upper arms. Some affected individuals have also reported weakness in muscles of the lower leg and foot called the dorsal foot extensors.

HMERF also causes severe weakness in muscles of the chest that are involved in breathing, particularly the diaphragm. This weakness leads to breathing problems and life-threatening respiratory failure.

Frequency

HMERF is a rare condition. It has been reported in several families of Swedish and French descent, and in at least one individual from Italy.

Genetic Changes

HMERF can be caused by a mutation in the *TTN* gene. This gene provides instructions for making a protein called titin. Titin plays an important role in muscles the body uses for movement (skeletal muscles) and in heart (cardiac) muscle.

Within muscle cells, titin is an essential component of structures called sarcomeres. Sarcomeres are the basic units of muscle contraction; they are made of proteins that generate the mechanical force needed for muscles to contract. Titin has several functions within sarcomeres. One of its most important jobs is to provide structure, flexibility, and stability to these cell structures. Titin also plays a role in chemical signaling and in assembling new sarcomeres.

The *TTN* gene mutation responsible for HMERF leads to the production of an altered version of the titin protein. Studies suggest that this change may disrupt titin's interactions with other proteins within sarcomeres and interfere with the protein's role in chemical signaling. Consequently, muscle fibers become damaged and weaken over time. It is unclear why these effects are usually limited to proximal muscles and muscles involved in breathing.

Some people with the characteristic features of HMERF do not have identified mutations in the *TTN* gene. In these cases, the genetic cause of the condition is unknown.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Edstrom myopathy
- HMERF
- MPRM
- myopathy, proximal, with early respiratory muscle involvement

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hereditary myopathy with early respiratory failure https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863599/

Other Diagnosis and Management Resources

- GeneReview: Hereditary Myopathy with Early Respiratory Failure (HMERF) https://www.ncbi.nlm.nih.gov/books/NBK185330
- National Heart, Lung, and Blood Institute: How Is Respiratory Failure Diagnosed? https://www.nhlbi.nih.gov/health/health-topics/topics/rf/diagnosis
- National Heart, Lung, and Blood Institute: How Is Respiratory Failure Treated? https://www.nhlbi.nih.gov/health/health-topics/topics/rf/treatment

General Information from MedlinePlus

- Diagnostic Tests https://medlineplus.gov/diagnostictests.html
- Drug Therapy https://medlineplus.gov/drugtherapy.html
- Genetic Counseling https://medlineplus.gov/geneticcounseling.html
- Palliative Care https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Muscle Disorders
  https://medlineplus.gov/muscledisorders.html
- Health Topic: Respiratory Failure
  https://medlineplus.gov/respiratoryfailure.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Congenital Myopathy
  https://www.ninds.nih.gov/Disorders/All-Disorders/Congenital-Myopathy-Information-Page

Educational Resources

- Disease InfoSearch: Hereditary myopathy with early respiratory failure
  http://www.diseaseinfosearch.org/Hereditary+myopathy+with+early+respiratory+failure/8524
- MalaCards: myopathy, proximal, with early respiratory muscle involvement
  http://www.malacards.org/card/myopathy_proximal_with_early_respiratory_muscle_involvement
- Merck Manual Home Edition for Patients and Caregivers: Respiratory Failure
  http://www.merckmanuals.com/home/lung-and-airway-disorders/respiratory-failure-and-acute-respiratory-distress-syndrome/respiratory-failure
- Orphanet: Hereditary proximal myopathy with early respiratory failure
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=178464

Patient Support and Advocacy Resources

- Congenital Muscle Disease International Registry
  https://www.cmdir.org/
- Muscular Dystrophy Association
  https://www.mda.org/
- Muscular Dystrophy Canada
  http://www.muscle.ca/
- Muscular Dystrophy UK
  http://www.musculardystrophyuk.org/
- Resource list from the University of Kansas Medical Center: Muscular Dystrophy / Atrophy
  http://www.kumc.edu/gec/support/muscular.html

GeneReviews

- Hereditary Myopathy with Early Respiratory Failure (HMERF)
  https://www.ncbi.nlm.nih.gov/books/NBK185330

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28hmerf%5BTIAB%5D%29+OR+%28%28dominant+myopathy%5BTIAB%5D%29+AND+%28early+respiratory+muscle%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- HEREDITARY MYOPATHY WITH EARLY RESPIRATORY FAILURE
  http://omim.org/entry/603689

Sources for This Summary

- Edström L, Thornell LE, Albo J, Landin S, Samuelsson M. Myopathy with respiratory failure and typical myofibrillar lesions. J Neurol Sci. 1990 May;96(2-3):211-28.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/2376753
- Lange S, Xiang F, Yakovenko A, Vihola A, Hackman P, Rostkova E, Kristensen J, Brandmeier B, Franzen G, Hedberg B, Gunnarsson LG, Hughes SM, Marchand S, Sejersen T, Richard I, Edström L, Ehler E, Udd B, Gautel M. The kinase domain of titin controls muscle gene expression and protein turnover. Science. 2005 Jun 10;308(5728):1599-603. Epub 2005 Mar 31.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15802564
- Nicolao P, Xiang F, Gunnarsson LG, Giometto B, Edström L, Anvret M, Zhang Z. Autosomal dominant myopathy with proximal weakness and early respiratory muscle involvement maps to chromosome 2q. Am J Hum Genet. 1999 Mar;64(3):788-92.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10053013
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1377796/
- Tasca G, Mirabella M, Broccolini A, Monforte M, Sabatelli M, Biscione GL, Piluso G, Gualandi F, Tonali PA, Udd B, Ricci E. An Italian case of hereditary myopathy with early respiratory failure (HMERF) not associated with the titin kinase domain R279W mutation. Neuromuscul Disord. 2010 Nov;20(11):730-4. doi: 10.1016/j.nmd.2010.07.269. Epub 2010 Aug 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20708934
- Xiang F, Nicolao P, Chapon F, Edström L, Anvret M, Zhang Z. A second locus for autosomal dominant myopathy with proximal muscle weakness and early respiratory muscle involvement: a likely chromosomal locus on 2q21. Neuromuscul Disord. 1999 Jul;9(5):308-12.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10407851

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